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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/194,053	11/23/98	CHOKRI M	USB96AKIDM

HM22/0619

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EXAMINER	
VANDER VEGT, F	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 06/19/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/194,053	Applicant(s) Chokri et al
	Examiner F. Pierre VanderVegt	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Oct 15, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), ~~or thirty days, whichever is longer,~~ from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *44-66, 75, 76, 80, and 81* ~~is~~/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *44-66, 75, 76, 80, and 81* ~~is~~/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

This application is a rule 371 continuation of PCT/EP97/02703.

Claims 44-66, 75, 76, 80 and 81 are currently pending in this application.

1. In view of the amendment filed April 4, 2000, only the following rejections are maintained.

Claim Rejections - 35 U.S.C. § 112

2. Claims 48, 52, 56, 57, 59, 60, 62-66, 75, 76, 80 and 81 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It was previously stated: "The claims are drawn to populations of monocyte-derived antigen presenting cells (MD-APCs) identified on the basis of the presence of particular cell surface antigens based upon mean intensity. The specification is not enabling for the isolation of the claimed cells for a multitude of reasons. First of all, the specification and claims fail to identify the fluorochrome used and the excitation wavelength at which fluorescence is detected. It is well established in the art that different fluorochromes, such as fluorescein, phycoerythrin, and TEXAS RED, have different intensities and optimally fluoresce at different wavelengths as measured in nanometers. Further, the specification does not identify the nature of the units used for the measurement of mean intensity fluorescence. Second, the specification and claims fail to identify the staining reagent adequately. Are the fluorochrome molecules attached to antigens specifically bound by the specified surface determinants or are they attached to antibodies specific for said surface determinants? Are the fluorochromes covalently bound to the antibody or antigen or is binding effected by indirect means, such as biotin-avidin affinity? Are the antibodies full length, Fab or $F(ab')_2$ fragments? In the absence of specifying standardized commercially available reagents, what is the molar ratio of the fluorochrome to the antigen/antibody/avidin? What staining conditions (temperature, light, time) are used? All of these variables would be recognized by one skilled in the art to be factors which directly influence mean intensity fluorescence. The specification states, for example, that FITC and PE labeled antibodies were used in working examples (page 16, for example), however fails to address any of the other variables inherent in the procedure of fluorescent staining and detection. In view of the insufficient guidance provided by the instant specification, it would not be possible for the artisan to reasonably predict the conditions needed to adequately identify the cells commensurate in scope with the claims and it would require a level of experimentation on the part of the practitioner which could not be considered routine.

In view of the nature of the invention, quantity of experimentation necessary, the level of the skilled artisan, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute."

Applicant's arguments filed April 4, 2000 have been fully considered but they are not persuasive.

Applicant argues that the fluorochrome used and the level of intensity, as expressed in unitless values, are not relevant to the enablement of the claimed invention. The Examiner respectfully disagrees with Applicant's position. First, in regard to the unitless values, there is no guidance provided to the practitioner regarding the level of intensity of the desired cells versus the intensity of a control. For example, in claim 48 ("mean intensity of about 100 to about 400") it is not clear what the level of the undesired control cell would be. Is the unitless value multiplicative, i.e., 100X to 400X the intensity of the control? Is the scale strictly numerical, i.e., what would the value of the control cell's value be, 0 to under 100? What if the control cell had an intensity of 200 on the unitless scale, what would the intensity value of a desired cell be, 201 to 400? While accepting the fact that unitless values are commonly used in the art, it is maintained that enablement for their use can only be achieved by also relating the intensity values of the control cell. Second, the fluorochrome used is important. It is apparent that the Examiner did not clearly articulate this point earlier and apologizes for the oversight. The fluorochrome is important for enablement for purposes of reproducibility. If the practitioner once uses FITC as the fluorochrome and in a separate procedure uses PE, how can the unitless values be correlated to one another, since the fluorochromes have different excitation wavelengths, can the values be directly correlated to one another? If two practitioners prefer the use of two different fluorochromes, can they directly correlate their results to one another and be sure of having the same population of cells? Accordingly, the issues of fluorochrome usage and correlation of unitless values are issues relevant to the enablement of the claims and the ground of rejection is maintained.

3. Claims 48, 52, 56, 57, 59, 60, 62-66, 75, 76, 80 and 81 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 48, 52, 56, 57, 59, 62 and 63 each recite "mean intensity" of a given range without specifying the units of measurement. Said mean intensities are a relative measurement but fail to identify the fluorochrome or to provide information as to whether they refer to a wavelength range within the cells fluoresce, a multiplier versus the intensity of some baseline or control or whether they refer to intensities upon some numerical scale which has been standardized.

4. **The following is a new ground of rejection not previously applied and this action is made NON-FINAL.**

Claim Rejections - 35 USC §§ 102 & 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 44-66, 75, 76, 80 and 81 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Unanue (U1 on form PTO-892).

The claims are broadly drawn to macrophages without clearly delineating a specific population thereof. The Unanue reference teaches that macrophages arise by the differentiation of monocytes (page 96, section "Origin and Distribution in particular). Unanue further teaches that macrophages are phagocytic, able to ingest microorganisms (page 99, second column in particular). Unanue also teaches that an immunological function of macrophages is to present antigen in context of MHC class II (page 101, section "Regulation of Class II MHC Expression" in particular). It is well known in the art that all cells in the body express MHC class I. Claim 45 is included because the term "high" is a relative term and does not serve to differentiate the intended population of macrophages from any other macrophages and claims 45, 47, 58, 61-66, 75, 76, 80 and 81 are included because the property of phagocytosing particulate antigens, such as formalin-fixed yeast, is an inherent property of macrophages which, in their role as antigen-presenting cells, can phagocytose particulate antigens in an antigen-independent manner, process the antigen and present antigenic fragments on their surface in the context of MHC class I and/or MHC class II for the antigen-specific stimulation of cytotoxic or helper T cells, respectively. Claims 48, 52, 56, 57, 59, 62-66, 75, 76, 80 and 81 are further included because the recited mean intensities of the markers are not expressed in units which would allow the practitioner to differentiate the instantly claimed MD-APCs from the wild-type cells isolated by the method of the Unanue reference. Therefore, the instantly claimed MD-APCs and the macrophages taught by Unanue appear to be the same or similar absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference between the materials, i.e., that the claims are directed to new materials and that such a difference would have been considered unexpected by one of ordinary skill in the art, that is, the claimed subject matter, if new, is unobvious.

In the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from those taught by the prior art and to establish patentable

differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

6. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2000 366-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. PIERRE VANDERVEGT
PATENT EXAMINER

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
June 16, 2000